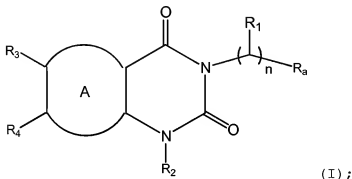


CLAIM AMENDMENTS

Please replace all prior versions and listings of claims with the amended claims as follows:

1. (Currently amended) A compound having formula (I):



wherein:

ring A is an aryl or heteroaryl ring wherein said aryl or heteroaryl ring is either unsubstituted or substituted with one or more substituents selected from halogen, $-R^o$, $-OR^o$, $-SR^o$, 1,2-methylene-dioxy, 1,2-ethylenedioxy; unsubstituted phenyl (Ph), unsubstituted $-O(Ph)$, unsubstituted $-CH_2(Ph)$, unsubstituted $-CH_2CH_2(Ph)$ or (Ph), $-O(Ph)$, $-CH_2(Ph)$, or $-CH_2CH_2(Ph)$ substituted with one or more $-R^o$ groups; $-NO_2$, $-CN$, $-N(R^o)_2$, $-NR^oC(O)R^o$, $-NR^oC(O)N(R^o)_2$, $-NR^oCO_2R^o$, $-NR^oNR^oC(O)R^o$, $-NR^oNR^oC(O)N(R^o)_2$, $-NR^oNR^oCO_2R^o$, $-C(O)C(O)R^o$, $-C(O)CH_2C(O)R^o$, $-CO_2R^o$, $-C(O)R^o$, $-C(O)N(R^o)_2$, $-OC(O)N(R^o)_2$, $-S(O)_2R^o$, $-SO_2N(R^o)_2$, $-S(O)R^o$, $-NR^oSO_2N(R^o)_2$, $-NR^oSO_2R^o$, $-C(=S)N(R^o)_2$, $-C(=NH)-N(R^o)_2$, or $-(CH_2)_qNHC(O)R^o$; wherein:

q is 0-2; and wherein:

each R^o is independently selected from hydrogen, a C_{1-6} aliphatic, wherein said C_{1-6} aliphatic group is either unsubstituted or substituted with one or more substituents selected from $=O$, $=S$, $=NNHR^s$, $=NN(R^s)_2$,

=NNHC(O)R⁺, =NNHCO₂(alkyl), =NNHSO₂(alkyl), =NR⁺NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, halogen, C₁₋₄ aliphatic, OH, O(C₁₋₄ aliphatic), NO₂, CN, CO₂H, CO₂(C₁₋₄ aliphatic), O(halo C₁₋₄ aliphatic), or halo C₁₋₄ aliphatic; an unsubstituted 5-6 membered heteroaryl or heterocyclic ring, phenyl, -O(Ph), or -CH₂(Ph), or wherein two occurrences of R⁰, on the same substituent or different substituents, taken together, form a 5-8-membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein:

each R⁺ is independently selected from hydrogen or a C₁₋₆ aliphatic group wherein said aliphatic group of R⁺ is either unsubstituted or substituted with one or more substituents selected from NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, halogen, C₁₋₄ aliphatic, OH, O(C₁₋₄ aliphatic), NO₂, CN, CO₂H, CO₂(C₁₋₄ aliphatic), O(halo C₁₋₄ aliphatic), or halo(C₁₋₄ aliphatic);

the nitrogen of any non-aromatic heterocyclic ring is either unsubstituted or substituted with one or more groups selected from -R⁺, -N(R⁺)₂, -C(O)R⁺, -OR⁺, -CO₂R⁺, -C(O)C(O)R⁺, -C(O)CH₂C(O)R⁺, -SO₂R⁺, -SO₂N(R⁺)₂, -C(=S)N(R⁺)₂, -C(=NH)-N(R⁺)₂, or -NR⁺SO₂R⁺; wherein:

R⁺ is hydrogen, an unsubstituted 5-6 membered heteroaryl or heterocyclic ring, an unsubstituted C₁₋₆ aliphatic, unsubstituted phenyl (Ph), unsubstituted -O(Ph), unsubstituted -CH₂(Ph), unsubstituted -CH₂CH₂(Ph); or C₁₋₆ aliphatic, phenyl(Ph), -O(Ph), -CH₂(Ph), or -CH₂CH₂(Ph) substituted with one or more groups selected from NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, halogen, C₁₋₄ aliphatic, OH, O(C₁₋₄ aliphatic), NO₂, CN, CO₂H, CO₂(C₁₋₄ aliphatic), O(halo C₁₋₄ aliphatic), or halo(C₁₋₄ aliphatic) or wherein two occurrences of R⁺, on the same substituent or different substituents, taken together, form a 5-8-membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from

nitrogen, oxygen, or sulfur;

R_3 is $-\text{COOH}$;

n is 0-4;

R_1 is H, or a hydroxyaliphatic, aminoaliphatic, aliphatic- COOH , aliphatic- CONH_2 , or arylaliphatic wherein said hydroxyaliphatic, aminoaliphatic, aliphatic- COOH , aliphatic- CONH_2 , or arylaliphatic is either unsubstituted or substituted with one or more substituents selected from halogen, $-\text{R}^\circ$, $-\text{OR}^\circ$, $-\text{SR}^\circ$, 1,2-methylene-dioxy, 1,2-ethylenedioxy; unsubstituted phenyl (Ph), unsubstituted $-\text{O}(\text{Ph})$, unsubstituted $-\text{CH}_2(\text{Ph})$, unsubstituted $-\text{CH}_2\text{CH}_2(\text{Ph})$ or (Ph), $-\text{O}(\text{Ph})$, $-\text{CH}_2(\text{Ph})$, or $-\text{CH}_2\text{CH}_2(\text{Ph})$ substituted with one or more $-\text{R}^\circ$ groups; $-\text{NO}_2$, $-\text{CN}$, $-\text{N}(\text{R}^\circ)_2$, $-\text{NR}^\circ\text{C}(\text{O})\text{R}^\circ$, $-\text{NR}^\circ\text{C}(\text{O})\text{N}(\text{R}^\circ)_2$, $-\text{NR}^\circ\text{CO}_2\text{R}^\circ$, $-\text{NR}^\circ\text{NR}^\circ\text{C}(\text{O})\text{R}^\circ$, $-\text{NR}^\circ\text{NR}^\circ\text{C}(\text{O})\text{N}(\text{R}^\circ)_2$, $-\text{NR}^\circ\text{NR}^\circ\text{CO}_2\text{R}^\circ$, $-\text{C}(\text{O})\text{C}(\text{O})\text{R}^\circ$, $-\text{C}(\text{O})\text{CH}_2\text{C}(\text{O})\text{R}^\circ$, $-\text{CO}_2\text{R}^\circ$, $-\text{C}(\text{O})\text{R}^\circ$, $-\text{C}(\text{O})\text{N}(\text{R}^\circ)_2$, $-\text{OC}(\text{O})\text{N}(\text{R}^\circ)_2$, $-\text{S}(\text{O})_2\text{R}^\circ$, $-\text{SO}_2\text{N}(\text{R}^\circ)_2$, $-\text{S}(\text{O})\text{R}^\circ$, $-\text{NR}^\circ\text{SO}_2\text{N}(\text{R}^\circ)_2$, $-\text{NR}^\circ\text{SO}_2\text{R}^\circ$, $-\text{C}(=\text{S})\text{N}(\text{R}^\circ)_2$, $-\text{C}(=\text{NH})-\text{N}(\text{R}^\circ)_2$, or $-(\text{CH}_2)_q\text{NHC}(\text{O})\text{R}^\circ$; wherein:

q is 0-2; and wherein:

each R° is independently selected from hydrogen, a C_{1-6} aliphatic, wherein said C_{1-6} aliphatic group is either unsubstituted or substituted with one or more substituents selected from $=\text{O}$, $=\text{S}$, $=\text{NNHR}^\circ$, $=\text{NN}(\text{R}^\circ)_2$, $=\text{NNHC}(\text{O})\text{R}^\circ$, $=\text{NNHCO}_2(\text{alkyl})$, $=\text{NNHSO}_2(\text{alkyl})$, $=\text{NR}^\circ\text{NH}_2$, $\text{NH}(\text{C}_{1-4}\text{aliphatic})$, $\text{N}(\text{C}_{1-4}\text{aliphatic})_2$, halogen, C_{1-4} aliphatic, OH , $\text{O}(\text{C}_{1-4}\text{aliphatic})$, NO_2 , CN , CO_2H , $\text{CO}_2(\text{C}_{1-4}\text{aliphatic})$, $\text{O}(\text{halo } \text{C}_{1-4}\text{aliphatic})$, or halo C_{1-4} aliphatic; an unsubstituted 5-6 membered heteroaryl or heterocyclic ring, phenyl, $-\text{O}(\text{Ph})$, or $-\text{CH}_2(\text{Ph})$, or wherein two occurrences of R° , on the same substituent or different substituents, taken together, form a 5-8-membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein:

each R^+ is independently selected from hydrogen or a C_{1-6} aliphatic group wherein said aliphatic group of R^+ is either unsubstituted or substituted with one or more substituents selected from NH_2 , $NH(C_{1-4}$ aliphatic), $N(C_{1-4}$ aliphatic) $_2$, halogen, C_{1-4} aliphatic, OH , $O(C_{1-4}$ aliphatic), NO_2 , CN , CO_2H , $CO_2(C_{1-4}$ aliphatic), $O(halo\ C_{1-4}$ aliphatic), or $halo(C_{1-4}$ aliphatic);

the nitrogen of any non-aromatic heterocyclic ring is either unsubstituted or substituted with one or more groups selected from $-R^+$, $-N(R^+)_2$, $-C(O)R^+$, $-OR^+$, $-CO_2R^+$, $-C(O)C(O)R^+$, $-C(O)CH_2C(O)R^+$, $-SO_2R^+$, $-SO_2N(R^+)_2$, $-C(=S)N(R^+)_2$, $-C(=NH)-N(R^+)_2$, or $-NR^+SO_2R^+$; wherein:

R^+ is hydrogen, an unsubstituted 5-6 membered heteroaryl or heterocyclic ring, an unsubstituted C_{1-6} aliphatic, unsubstituted phenyl (Ph), unsubstituted $-O(Ph)$, unsubstituted $-CH_2(Ph)$, unsubstituted $-CH_2CH_2(Ph)$; or C_{1-6} aliphatic, phenyl(Ph), $-O(Ph)$, $-CH_2(Ph)$, or $-CH_2CH_2(Ph)$ substituted with one or more groups selected from NH_2 , $NH(C_{1-4}$ aliphatic), $N(C_{1-4}$ aliphatic) $_2$, halogen, C_{1-4} aliphatic, OH , $O(C_{1-4}$ aliphatic), NO_2 , CN , CO_2H , $CO_2(C_{1-4}$ aliphatic), $O(halo\ C_{1-4}$ aliphatic), or $halo(C_{1-4}$ aliphatic) or wherein two occurrences of R^+ , on the same substituent or different substituents, taken together, form a 5-8-membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

R_2 is an unsubstituted aliphatic, or a cycloaliphatic-aliphatic[[,]] or heteroarylaliphatic, wherein said ~~aliphatic~~, cycloaliphatic-aliphatic[[,]] or heteroarylaliphatic[[, or]] is either unsubstituted or substituted with one or more substituents selected from halogen, $-R^0$, $-OR^0$, $-SR^0$, 1,2-methylene-dioxy, 1,2-ethylenedioxy; unsubstituted phenyl (Ph), unsubstituted $-O(Ph)$, unsubstituted $-CH_2(Ph)$, unsubstituted $-CH_2CH_2(Ph)$ or (Ph), $-O(Ph)$, $-CH_2(Ph)$, or $-CH_2CH_2(Ph)$ substituted with one or more $-R^0$ groups; $-NO_2$, $-CN$, $-N(R^0)_2$, $-NR^0C(O)R^0$,

-NR^oC(O)N(R^o)₂, -NR^oCO₂R^o, -NR^oNR^oC(O)R^o, -NR^oNR^oC(O)N(R^o)₂,
 -NR^oNR^oCO₂R^o, -C(O)C(O)R^o, -C(O)CH₂C(O)R^o, -CO₂R^o, -C(O)R^o,
 -C(O)N(R^o)₂, -OC(O)N(R^o)₂, -S(O)₂R^o, -SO₂N(R^o)₂, -S(O)R^o,
 -NR^oSO₂N(R^o)₂, -NR^oSO₂R^o, -C(=S)N(R^o)₂, -C(=NH)-N(R^o)₂, or
 -(CH₂)_qNHC(O)R^o; wherein:

q is 0-2; and wherein:

each R^o is independently selected from hydrogen, a C₁₋₆ aliphatic, wherein said C₁₋₆ aliphatic group is either unsubstituted or substituted with one or more substituents selected from =O, =S, =NNHR^{*}, =NN(R^{*})₂, =NNHC(O)R^{*}, =NNHCO₂(alkyl), =NNHSO₂(alkyl), =NR^{*}NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, halogen, C₁₋₄ aliphatic, OH, O(C₁₋₄ aliphatic), NO₂, CN, CO₂H, CO₂(C₁₋₄ aliphatic), O(halo C₁₋₄ aliphatic), or halo C₁₋₄ aliphatic; an unsubstituted 5-6 membered heteroaryl or heterocyclic ring, phenyl, -O(Ph), or -CH₂(Ph), or wherein two occurrences of R^o, on the same substituent or different substituents, taken together, form a 5-8-membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein:

each R^{*} is independently selected from hydrogen or a C₁₋₆ aliphatic group wherein said aliphatic group of R^{*} is either unsubstituted or substituted with one or more substituents selected from NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, halogen, C₁₋₄ aliphatic, OH, O(C₁₋₄ aliphatic), NO₂, CN, CO₂H, CO₂(C₁₋₄ aliphatic), O(halo C₁₋₄ aliphatic), or halo(C₁₋₄ aliphatic);

the nitrogen of any non-aromatic heterocyclic ring is either unsubstituted or substituted with one or more groups selected from -R⁺, -N(R⁺)₂, -C(O)R⁺, -OR⁺, -CO₂R⁺, -C(O)C(O)R⁺, -C(O)CH₂C(O)R⁺, -SO₂R⁺, -SO₂N(R⁺)₂, -C(=S)N(R⁺)₂, -C(=NH)-N(R⁺)₂, or -NR⁺SO₂R⁺; wherein: R⁺ is hydrogen, an unsubstituted 5-6 membered heteroaryl or heterocyclic ring, an unsubstituted C₁₋₆ aliphatic,

unsubstituted phenyl (Ph), unsubstituted -O(Ph), unsubstituted -CH₂(Ph), unsubstituted -CH₂CH₂(Ph); or C₁₋₆ aliphatic, phenyl(Ph), -O(Ph), -CH₂(Ph), or -CH₂CH₂(Ph) substituted with one or more groups selected from NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, halogen, C₁₋₄ aliphatic, OH, O(C₁₋₄ aliphatic), NO₂, CN, CO₂H, CO₂(C₁₋₄ aliphatic), O(halo C₁₋₄ aliphatic), or halo(C₁₋₄ aliphatic) or wherein two occurrences of R¹, on the same substituent or different substituents, taken together, form a 5-8-membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

R³ and R⁴ are independently selected from R¹¹, R¹², R¹⁴ or R¹⁵;

wherein:

each R¹¹ is independently selected from 1,2-methylenedioxy, 1,2-ethylenedioxy, R⁶ or (CH₂)_m-Y;

wherein m is 0, 1 or 2; and

Y is selected from halogen, CN, NO₂, CF₃, OCF₃, OH, SR⁶, S(O)R⁶, SO₂R⁶, NH₂, NHR⁶, N(R⁶)₂, NR⁶R⁸, COOH, COOR⁶ or OR⁶;

each R¹² is independently selected from (C₁-C₆)-straight or branched alkyl, or (C₂-C₆)-straight or branched alkenyl or alkynyl; and each R¹² optionally comprises up to 2 substituents, wherein:

the first of said substituents, if present, is selected from R¹¹, R¹⁴ and R¹⁵, and

the second of said substituents, if present, is R¹¹;

each R¹⁴ is independently selected from OR¹⁵, OC(O)R⁶, OC(O)R¹⁵, OC(O)OR⁶, OC(O)OR¹⁵, OC(O)N(R⁶)₂, OP(O)(OR⁶)₂, SR⁶, SR¹⁵, S(O)R⁶, S(O)R¹⁵, SO₂R⁶, SO₂R¹⁵, SO₂N(R⁶)₂, SO₂NR¹⁵R⁶, SO₃R⁶, C(O)R¹⁵, C(O)OR¹⁵, C(O)R⁶,

C(O)OR⁶, NC(O)C(O)R⁶, NC(O)C(O)R¹⁵, NC(O)C(O)OR⁶,
 NC(O)C(O)N(R⁶)₂, C(O)N(R⁶)₂, C(O)N(OR⁶)R⁶, C(O)N(OR⁶)R¹⁵,
 C(NOR⁶)R⁶, C(NOR⁶)R¹⁵, N(R⁶)₂, NR⁶C(O)R¹¹, NR⁶C(O)R⁶,
 NR⁶C(O)R¹⁵, NR⁶C(O)OR⁶, NR⁶C(O)OR¹⁵, NR⁶C(O)N(R⁶)₂,
 NR⁶C(O)NR¹⁵R⁶, NR⁶SO₂R⁶, NR⁶SO₂R¹⁵, NR⁶SO₂N(R⁶)₂,
 NR⁶SO₂NR¹⁵R⁶, N(OR⁶)R⁶, N(OR⁶)R¹⁵, P(O)(OR⁶)N(R⁶)₂, and
 P(O)(OR⁶)₂;

each R¹⁵ is a cycloaliphatic, aryl,
 heterocyclyl, or heteroaromatic; and each R¹⁵ optionally
 comprises up to 3 substituents, each of which, if
 present, is R¹¹;

each R⁶ is independently selected from H,
 (C₁-C₆)-straight or branched alkyl, or (C₂-C₆) straight
 or branched alkenyl; and each R⁶ optionally comprises a
 substituent that is R⁷;

R⁷ is a cycloaliphatic, aryl, heterocyclyl, or
 heteroaromatic; and each R⁷ optionally comprises up to 2
 substituents independently chosen from H, (C₁-C₆)-
 straight or branched alkyl, (C₂-C₆) straight or branched
 alkenyl, 1,2-methylenedioxy, 1,2-ethylenedioxy, or
 (CH₂)_p-Z;

wherein p is 0, 1 or 2; and

Z is selected from halogen, CN, NO₂, CF₃, OCF₃,
 OH, S(C₁-C₆)-alkyl, SO(C₁-C₆)-alkyl, SO₂(C₁-C₆)-alkyl,
 NH₂, NH(C₁-C₆)-alkyl, N((C₁-C₆)-alkyl)₂, N((C₁-C₆)-
 alkyl)R⁸, COOH, C(O)O(C₁-C₆)-alkyl or O(C₁-C₆)-alkyl; and

R⁸ is ~~an amino protecting group~~ -C(O)CH₃,
-C(O)Ph or -SO₂Ph;

provided that:

R³ and R⁴ are not simultaneously hydrogen;

when R³ is H, then R⁴ is not chloro; and
when R⁴ is H, then R³ is not -SCH₃ or -NH-C(O)CH₃.

2. (Original) The compound according to claim 1, wherein ring A is an optionally substituted 5 or 6 membered aryl or heteroaryl ring, wherein said heteroaryl ring contains up to 2 ring heteroatoms independently selected from O, S, or NH.

3. (Original) The compound according to claim 2, wherein ring A is phenyl.

4. (Original) The compound according to claim 1, wherein R₁ is hydrogen, -(CH₂)_q-X, wherein q is 1-4, and X is OH, NH₂, COOH or CONH₂, (C1-C6)-alkyl, or benzyl.

5. (Previously amended) The compound according to claim 4, wherein R₁ is hydrogen, hydroxymethyl, methyl, -CH₂COOH, -CH₂CONH₂, aminobutyl, or isopentyl.

6. (Currently amended) The compound according to claim 1, wherein R₂ is selected from butyl, isobutyl, ~~methoxypropyl~~, cyclopentyl, cyclohexylmethyl, pyridylmethyl, furanylmethyl, or thienylmethyl.

7. (Previously amended) The compound according to claim 6, wherein R₂ is selected from 2-furanylmethyl.

8. (Canceled)

9. (Previously amended) A pharmaceutical composition comprising a compound according to any one of claims 1-7 and 17-18 and a pharmaceutically acceptable adjuvant or carrier.

10. (Withdrawn) A method for treating or lessening

the severity of a disease in a patient, wherein said disease is selected from autoimmune diseases, proliferative diseases, angiogenic disorders, or cancers, said method comprising the step of administering to said patient a composition according to claim 9.

11. (Withdrawn) A method for treating or lessening the severity of a SHP-2-mediated disease or condition in a patient comprising the step of administering to said patient a composition according to claim 9.

12. (Withdrawn) The method according to claim 10, wherein said autoimmune disease is selected from glomerulo-nephritis, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Graves' disease, autoimmune gastritis, diabetes, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, psoriasis, or graft vs. host disease.

13. (Withdrawn) The method according to claim 10, wherein said proliferative disease is selected from acute myelogenous leukemia, chronic myelogenous leukemia, metastatic melanoma, Kaposi's sarcoma, multiple myeloma or HTLV-1-mediated tumorigenesis.

14. (Withdrawn) The method according to claim 10, wherein said angiogenic disorder is selected from solid tumors, ocular neovascularization, or infantile haemangiomas.

15. (Withdrawn) The method according to claim 10, wherein said cancers is selected from colon cancer, breast cancer, stomach cancer, or ovarian cancers.

16. (Withdrawn-previously amended) An implantable medical device coated with a compound according to any one of claims 1-7 and 17-18, wherein said device is selected from prostheses, artificial valves, vascular grafts, stents or catheters.

17. (Previously presented) The compound according to claim 1 wherein R_3 and R_4 are independently selected from hydrogen, halo, acetamido, allyloxy, thiophenyl, sulfoxyalkyl, or sulfoxyphenyl.

18. (Previously presented) A compound according to claim 1 selected from:

